

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
23 September 2004 (23.09.2004)

PCT

(10) International Publication Number
WO 2004/080376 A2

- (51) International Patent Classification⁷: A61K
- (21) International Application Number:
PCT/EP2004/002644
- (22) International Filing Date: 11 March 2004 (11.03.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
0305918.5 14 March 2003 (14.03.2003) GB
- (71) Applicant (for all designated States except US): **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford Middlesex UB6 0NN (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **DEMONT, Emmanuel, Hubert** [FR/GB]; GlaxoSmithKline, The Frythe, Welwyn Hertfordshire AL6 9AR (GB). **REDSHAW, Sally** [GB/GB]; GlaxoSmithKline, The Frythe, Welwyn Hertfordshire AL6 9AR (GB). **WALTER, Daryl, Simon** [GB/GB]; GlaxoSmithKline, The Frythe, Welwyn Hertfordshire AL6 9AR (GB).
- (74) Agent: **GIBSON, Mark**; GlaxoSmithKline (CN925.1), 980 Great West Road, Brentford Middlesex TW8 9GS (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/080376 A2

(54) Title: NOVEL COMPOUNDS

(57) Abstract: The present invention relates to novel hydroxyethylamine compounds having Asp2 (β -secretase, BACE1 or Memapsin) inhibitory activity, processes for their preparation, to compositions containing them and to their use in the treatment of diseases characterised by elevated β -amyloid levels or β -amyloid deposits, particularly Alzheimer's disease.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference MXG-PB60133	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/EP2004/002644	International filing date (day/month/year) 11/03/2004	(Earliest) Priority Date (day/month/year) 14/03/2003
Applicant GLAXO GROUP LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

HYDROXYETHYLAMINE COMPOUNDS HAVING ASP2 INHIBITORY ACTIVITY FOR THE TREATMENT OF ALZHEIMER'S DISEASE

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regards to the drawings,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/2004/002644

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C311/08 C07C317/36 C07C323/36 C07D207/27 C07D209/42
 C07D213/75 C07D231/12 A61K31/18 A61K31/275 A61K31/402
 A61K31/404 A61K31/415 A61K31/425 A61K31/4402 A61K31/4406

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data, PAJ, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/02505 A (ELAN PHARM INC) 10 January 2002 (2002-01-10) cited in the application page 69, line 31 - page 76, line 31; claim 1 -----	1-8

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

18 August 2004

Date of mailing of the international search report

21/09/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Cooper, S

INTERNATIONAL SEARCH REPORT

International Application No
PCT/022004/002644

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/002644

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 7 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP2004/002644

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0202505	A	10-01-2002	AU 7168601 A	14-01-2002
			AU 7309401 A	14-01-2002
			AU 7311301 A	14-01-2002
			AU 7313201 A	14-01-2002
			AU 7313701 A	14-01-2002
			BR 0111980 A	06-05-2003
			BR 0112000 A	03-06-2003
			CA 2410651 A1	10-01-2002
			CA 2410680 A1	10-01-2002
			CA 2410972 A1	10-01-2002
			CN 1447789 T	08-10-2003
			CN 1443155 T	17-09-2003
			CZ 20024194 A3	14-01-2004
			EE 200200716 A	16-08-2004
			EP 1299349 A2	09-04-2003
			EP 1299352 A2	09-04-2003
			EP 1353898 A2	22-10-2003
			HU 0303037 A2	01-03-2004
			JP 2004502664 T	29-01-2004
			JP 2004502665 T	29-01-2004
			JP 2004502669 T	29-01-2004
			NO 20026199 A	21-02-2003
			SK 18442002 A3	07-07-2004
			WO 0202505 A2	10-01-2002
			WO 0202518 A2	10-01-2002
			WO 0202506 A2	10-01-2002
			WO 0202520 A2	10-01-2002
			WO 0202512 A2	10-01-2002
			US 2002143177 A1	03-10-2002
			US 2003096864 A1	22-05-2003
			US 2002128255 A1	12-09-2002
			US 2002016320 A1	07-02-2002